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10/580,485	05/24/2006	Joachim Moormann	RO4246US (#90568)	2532

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EXAMINER	
PALENIK, JEFFREY T	
ART UNIT	PAPER NUMBER
1615	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,485	MOORMANN ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *16-24 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 25-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :24 May 2006,14 June 2007 and 30 July 2007 .

DETAILED ACTION

RESPONSE TO REMARKS

The Examiner thanks the Applicants for their timely reply filed on 21 May 2008, in the matter of 10/580,485.

Applicants' election **with traverse** of Group I (claims 1-15 and 25-37) is acknowledged. Applicants traverse the lack of unity requirement on the grounds that the Examiner has not shown the that which appears to be sufficient to illustrate the single inventive concept unique to both sets of claims, namely that Asmussen "fails to provide any indication that oral administration forms may be present in the form of a film" and that Asmussen "pertains to conventional oral forms, such as tablets, capsules, [etc.]".

Applicants' request for reconsideration of the restriction requirement has been fully considered by the Examiner and **is persuasive**. However, upon further consideration of the claims submitted by Applicants, a new requirement follows. Regardless, the claims still do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same corresponding technical feature. There is no special technical feature since claims 6 and 10 of Asmussen et al. (USPN 6,599,511 or WO 00/48582) teach the instantly claimed reservoir layered oral transdermal pharmaceutical preparation comprising the instantly claimed active desoxypeganine. The administration composition is further taught as comprising film-shaped (i.e. membrane) semi-permeable release layers (col. 3, lines 9-12).

Claims 16-24 and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or

linking claim. Applicants timely traversed the restriction requirement between the compositions and methods.

The remaining claims 1-15 and 25-37 are presented and represent all claims under consideration.

INFORMATION DISCLOSURE STATEMENT

Three Information Disclosure Statements (IDS) filed 24 May 2008, 14 June 2007 and 30 July 2007 is acknowledged and has been reviewed.

SPECIFICATION

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

CLAIM REJECTIONS - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter that is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 14 is drawn to a limitation to the composition of claim 1, wherein said composition "additionally contains at least one further pharmaceutically active substance which is not selected from the group consisting of deoxypeganine, deoxypeganine derivatives and salts of deoxypeganine and deoxypeganine derivatives".

While the Examiner acknowledges that the aforementioned limitation is mentioned in the instant specification (pg. 4, ¶3), the limitation is not defined by the instant specification in a clear and concise manner so as to specifically depict or further define which additional pharmaceutically active substances may be incorporated. As such, the disclosure of the instant specification is not sufficient to support of the generic concept of "at least one further pharmaceutically active substance which is not selected from…" as a limitation to be considered with regards to the instantly claimed dosage form of use and requires further clarification. Herein and the purposes of examination on the merits, the Examiner broadly interprets the limitation "technical processes" to mean any additional pharmaceutically active substance which may be incorporated into a film-shaped oral mucosa delivery composition, such as galanthamine (see US PGPub N° 2007/01900117, Abstract).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 and 25-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation "at least one of the active substance deoxypeganine and a deoxypeganine derivative", as recited in claim 1 renders the claims indefinite due to the grammar used in the claim. Read broadly, the Examiner reasonably interprets the limitation as reciting that the medicament contains at least one from the group of the actives listed as

deoxypeganine and deoxypeganine derivatives (i.e. a small Markush group). Herein, for the purposes of examination, the Examiner interprets as such.

Claim 6 recites the limitation "the content of said at least one active substance..." in lines of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claims 12 and 37 are rendered indefinite due the recitation of the medicament having either a "depot effect" or "release[ing]" said active over a period of time. The recitation is not clear since it can not be clearly discerned whether the active is to be (1) stored for the claimed periods of time prior to release or (2) released from the dosage over the claimed periods of time. Herein and for the purposes of examination on the merits, the Examiner broadly and reasonable interprets the limitation as reciting releasing the active over a period of time between 8-24 hours.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present

instance, claim 5 recites the broad recitation "multilayer structure", and the claim also recites "two- and three-layer structure" which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 8 recites the broad recitation "is mucoadhesive", and the claim also recites "has a mucoadhesive outer surface" which is the narrower statement of the range/limitation.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5, 14, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asmussen et al. (US Pre-Grant Publication N° 2007/0190117) in combination with Asmussen et al. (USPN 6,599,511).

The instant claims are drawn to an orally administered, film-shaped medicament containing at least one of the active substances: deoxypeganine and a deoxypeganine derivative such as an acid salt derivative (claims 1, 2 and 25). Claims 3 and 26 further limits the dosage form to an oral transmucosal (i.e. buccal) administration form. The structure of the dosage form is recited as having multiple layers (claim 5). Claim 14, as discussed above,

further limits the composition of claim 1 such that it additionally contains a non-deoxypeganine-based active substance, such as galanthamine.

The Pre-Grant Publication to Asmussen (also herein referred to as the '117 application) expressly teaches a film-shaped medicament for buccal administration of galanthamine and at least one further pharmaceutically active substance, which is preferably selected from the group comprising acetylcholinesterase inhibitors (Abstract and claim 10). The Abstract and claim 7 also teach that the film-shaped medicament has a bilayer or multilayer structure, wherein at least one of the layers contains the active substance. However, the '117 application does not further teach any specific examples acetylcholinesterase inhibitors which may be incorporated into said film-shaped dosage form.

The '511 patent to Asmussen et al. expressly teaches using the compound desoxypeganine (1,2,3,9-tetrahydropyrrolo[2,1-b] quinazoline; deoxypeganine), which is a noted inhibitor of acetylcholinesterase (col. 1, lines 42-52), in orally, transdermally or sublingually (e.g. buccal) administered pharmaceutical preparations (claim 6 and col. 1, lines 18-20). Claim 6 further teaches that the desoxypeganine-based active compound consists of desoxypeganine and/or a pharmaceutically acceptable salt thereof such as the hydrochloride salt (col. 1, line 63 to col. 2, line 3). The dosage form is further taught as comprising multiple layers, including a reservoir layer containing said desoxypeganine-based active substance(s) (claim 10 and col. 2, lines 38-49).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a buccally-administrable, film-shaped dosage form comprising an

acetylcholinesterase inhibitor such as deoxypeganine and/or its hydrochloride salt, and at least one other non-deoxypeganine-based active compound such as galanthamine as taught and suggested by Asmussen ('117) and Asmussen ('511).

Since both of the inventions to Asmussen overlap in their teachings, as discussed above, one of ordinary skill in the art would have been particularly motivated to prepare the instantly claimed composition. Thus, it would have been *prima facie* obvious to combine the teachings provided by the two dosage forms, each of which are taught by the art as being useful for the same purpose, in order to form a third composition, such as that which is instantly claimed, to be used for the very same purpose; the idea of combining them flowing logically from their having been individually taught in the prior art (MPEP §2144.06). In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)

Claims 4, 6-13, 15 and 27-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Asmussen et al. ('117) and Asmussen et al. ('511).

With respect to claims 1-3, 5, 14, 25 and 26, already discussed above, claims 4, 6, and 27-29 recite percent weight limitations for the deoxypeganine-based active substance(s) within the reservoir layer (claims 4, 27 and 28) and/or the dosage form as a whole (claims 6 and 29).

Asmussen ('117) expressly teaches in claim 2 that the active substance resides in a reservoir within at least one of the layers at a particularly preferred percent range of 20-50% by weight. Claim 9 teaches that the active substance content of the dosage form is preferably

between 1-20% by weight of the form. However, the '117 application does not expressly teach that the acetylcholinesterase inhibitor active compounds contribute to these percentages or if they do, it is not expressly taught how much is attributed to said inhibitors.

Asmussen ('115) on the other hand, expressly teaches the multilayered dosage form as comprising a preferred percent weight range of 5-20% by weight of the desoxypeganine-based active (col. 2, lines 61-65). Since only one reservoir layer is described in the delivery device, said layer containing the desoxypeganine-based drug, it then follows that the overall device contains the claimed amount of active as well.

The primary reference ('117) does not expressly teach the percent weight ranges of desoxypeganine-based active either within the reservoir layer or the overall medicament, as claimed by Applicants. However, since the values and formats of each parameter with respect to the claimed composition are adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. In the instant case, under the guidance of the '511 patent, which teaches the presence of the desoxypeganine-based active in the compositional percentages as instantly claimed, it would have been *prima facie* obvious to customize the amount of acetylcholinesterase inhibitor within the film-shaped galanthamine medicament ('117) such that the levels of desoxypeganine-based active of the instantly claimed medicament were met. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of this parameter would have been obvious at the time of Applicants' invention.

With respect to claims 1-3, 5, 14, 25 and 26, already discussed above, limitations to the overall thickness of the film composition are recited (claims 7, 30 and 31). The composition is recited as being mucoadhesive (claim 8). The composition is recited as being soluble in an aqueous media such as saliva (claims 9, 32, 33 and 36). With regard to the limitations recited in claims 9 and 33, which respectively state that "dissolution takes place between 1 second and 5 minutes" and "…between 3-30 seconds"; until some material difference in the properties of the composition is demonstrated, said limitations are considered by the Examiner to be directed toward the film-shaped formulation, which is instantly claimed. The composition is also recited as being disintegratable in an aqueous media such as saliva (claims 10, 34 and 35). Similar to the dissolution property, regarding the limitations of claims 10 and 35wherein "dissolution takes place between 1 second and 5 minutes" and "…between 3-30 seconds"; until some material difference in the properties of the composition is demonstrated, said limitations are considered by the Examiner to be directed toward the film-shaped formulation, which is instantly claimed. Claims 12 and 37, as discussed above, recite that the active agent is released between 8-24 hours. Claim 13 further limits the composition of claim 1 such that it comprises at least one active rapid-release layer and at least one active delayed-release layer. Claim 15 recites that the composition of claim 1 further contains at least one auxiliary substance (i.e. excipients, additives, etc.).

Asmussen ('117) expressly teaches the following of Applicants' claimed parameters:

- that the flat film-shaped medicaments are taught as having a preferred layer thickness in the range of 0.01-5 mm ¶[0023],

- preferred embodiments of the film-shaped dosage form are taught whereby said preparations are characterized as being mucoadhesive and soluble in aqueous media, being mucoadhesive and disintegratable in aqueous media, or being mucoadhesive and capable of gelling or swelling in aqueous media ¶[0041],
- aqueous media is further taught as being physiological media and is understood to mean water and physiological media such as saliva ¶[0038],
- disintegration time for the dosage form is taught as being between 10 seconds and 12 ¶[0042],
- the active substance-containing layer of the wafers, or at least one of the layers is taught as having a delayed active release ranging up to a preferred duration of 24 hours ¶[0050],
- having an outer release layer which is followed distally (i.e. away from the buccal contact surface) by at least one further layer which preferably exhibits a retarded active substance release ¶[0051],
- the film-shaped medicament is further characterized such that it contains one or more auxiliaries such as fillers, colorants, emulsifiers, plasticizers, disintegration promoters, disintegrants (wick agents), wetting agents, sweetening and flavoring agents, preservatives, pH regulators, permeation-enhancing substances and antioxidants (claim 12 and ¶¶[0053]-[0055])

In view of the combined teachings of Asmussen '117 and '511, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a film-

shaped dosage form comprising a deoxypeganine-based active and at least one other active such as galanthamine as taught and suggested by Asmussen ('117) and Asmussen ('511), and format the structure of said dosage form as expressly taught by Asmussen ('117), to produce the instantly claimed composition.

Since both of the inventions to Asmussen overlap in their teachings, as discussed above, one of ordinary skill in the art would have been motivated to prepare the instantly claimed composition, and would have been particularly motivated to incorporate compounds such as deoxypeganine hydrochloride into the invention practiced by Asmussen ('117) alongside a non-deoxypeganine compound such as galanthamine, as active substances for the resulting oral film-shaped dosage form. Thus, it would have been *prima facie* obvious to combine the teachings provided by the two dosage forms, each of which are taught by the art as being useful for the same purpose, in order to form a third composition, such as that which is instantly claimed, to be used for the very same purpose; the idea of combining them flowing logically from their having been individually taught in the prior art (MPEP §2144.06). In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)

From the teachings of the combined references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

All claims have been rejected; no claims are allowed.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615